International Journal of Surgery 9 (2011) 113–116

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.theijs.com

Editorial

Central nervous system infections and the neurosurgeon: A perspective

Central nervous system (CNS) infections and their sequalae still constitute a major source of morbidity. In the recent past, the introduction of newer broad spectrum antibiotics, improved imaging technology and intensive care facilities have significantly altered the natural history of central nervous system infections. It is well known that brain does not have an immune system of its own and an intact blood brain barrier is largely impervious to infections. It is exemplified by the fact that CNS infections are uncommon compared to a large proportion of patients inflicted with septicemia or pyemia.

Brain abscess is one of the most serious diseases of the central nervous system. This condition is more common among men – twice to three times, and morbidity rate is highest in fourth decade of the life.[1,2] Brain abscess still continues to be a significant problem in the developing world due to large scale poverty, illiteracy and lack of hygiene. Brain abscess resulting from acute bacterial meningitis is rare. Otogenic cerebellar/temporal lobe abscesses are common in children due to chronic active suppurative otitis media while fungal abscesses are seen more commonly in adult patients with immunocompromised status.

Advanced magnetic resonance (MR) imaging has revolutionized the diagnosis of brain abscess. Diffusion weighted imaging (DWI) usually show restricted diffusion (bright signal) that helps to differentiate abscesses from necrotic neoplasms, which are not usually restricted,[3] although not all abscesses follow this rule. DWI has a sensitivity and specificity of over 90% for distinguishing epidermoid which has low apparent diffusion coefficient (ADC) from arachnoid cyst (high ADC) and distinguishing abscess (low ADC) from necrotic tumor (high ADC). Magnetic resonance spectroscopy has been shown to be specifically beneficial in differentiating between brain abscesses and other cystic lesions, which can be used to expedite implementation of the appropriate antimicrobial therapy.[4,5] Proton magnetic resonance spectroscopy (1H-MRS) can detect a choline resonance that is largely due to glycerophosphocholine. 1H-MRS is a safe, non-invasive imaging modality and can accurately differentiate between necrotic/cystic tumor and cerebral abscesses.[5] 1H-MRS can also provide valuable information regarding the etiology of an abscess, as well as, its response to any medical or surgical treatment.

The pia arachnoid membrane tends to serve as an effective barrier to the spread of infection into the brain tissue. The abscess wall is crucial in maintaining the integrity of the brain function and limits the expansion of the infective process. At 3–4 weeks, the abscess capsule becomes thick and is amenable to excision. There is minimal risk of perforation and the possibility of its complete separation from the brain parenchyma. Antibiotics help eradicate the infection and the abscess wall involutes itself, sometimes leaving no evidence of its occurrence. In most instances, aspiration of the purulent material is sufficient to initiate the healing of abscess. However, surgical excision becomes mandatory if the pus is thick and in multiloculated abscesses. Urgent evacuation of abscess is required for subdural empyema and cerebellar abscess. Computed tomography (CT) guided stereotactic aspiration is particularly advocated in management of deep-seated abscesses, multiple abscesses, and abscesses located in eloquent areas of the brain. The technique of fiber tracking based on diffusion tensor imaging offers the unique possibility of localizing the white matter pathways of the brain in vivo.[6] In patients with cerebral tumors or space-occupying lesions of the brain, these pathways are often damaged or significantly displaced. Knowledge of the exact location of the lesion with respect to clinically eloquent white matter pathways is of great value to the neurosurgeon in planning the appropriate surgical strategy. A traumatic brain abscess may require craniotomy to remove foreign material or bone chips. Cerebellar or brain stem abscesses are often indication for posterior fossa craniotomy since there is high risk of brain herniation due to the small volume of posterior fossa.[1,2] Periventricular brain abscesses often require craniotomy given the risk of intraventricular rupture. A ventriculostomy placement is indicated for significantly elevated intracranial pressure. There is no well-controlled, randomized clinical study evaluating the use of corticosteroids for controlling the cerebral edema surrounding brain abscess. However, corticosteroids are recommended perioperatively for reducing intracranial pressure and avoiding acute brain herniation.[7] Tuberculous brain abscess is rare and can be difficult to differentiate from pyogenic abscess. It results from the caseation of tuberculoma and pus formation due to polymorphnuclear infiltration. The wall is thicker than pyogenic abscess. Antituberculous therapy along with aspiration of the abscess is advocated. Stereotactic aspiration of the abscess can be performed but there is a risk of neurological worsening and flaring up of tuberculous lesion and hence caution is advised.[8] There is a resurgence of multidrug resistant tuberculosis due to high prevalence of Human Immunodeficiency virus (HIV) and other immunodeficiency states. Tuberculosis in HIV infected patients should be treated within specialist units by physicians with expertise in both HIV and tuberculosis, or in a combined approach between HIV and tuberculosis experts.[9]

The most important factors influencing mortality from intracranial abscess are age and neurological condition of the patient at the time of admission. Delays in hospitalization, focal neurologic

1743-9191/$ – see front matter
doi:10.1016/j.ijsu.2010.11.001

deficits at admission, impaired host immunity, uncontrolled diabetes, and Glasgow Coma Scale less than 12 are associated with death and permanent neurologic deficits because of brain abscesses.[1] The treatment of brain abscess necessitates a multidisciplinary approach, including neuroradiological evaluation, surgical intervention, use of antibiotics and eradication of primary infected foci. Despite the usage of antibiotics, the incidence of brain abscess is exceedingly low. Broad spectrum coverage including a fourth-generation cephalosporin, metronidazole, and vancomycin, based on predisposing factors can be administered till the pus culture report is available. Carbapenems can be used in place of the combination of cephalosporins and metronidazole. Once a causative microorganism is identified, antimicrobial therapy can be tailored. Similar to meningitis, the choice of optimal therapy is determined by antimicrobial penetration to the brain parenchyma and in vitro susceptibilities of the pathogens. While at least 6–8 weeks of parenteral therapy has been traditionally given for bacterial brain abscesses, there is no convincing data supporting the optimal duration of therapy. Duration of antimicrobial therapy should be determined individually, based on the size of abscess, combination of surgical treatment, causative organism and response to treatment.

The treatment of tuberculous meningitis (TBM) is predominantly antituberculous chemotherapy. Empirical anti-tuberculosis therapy should be started promptly in all patients in whom the diagnosis of TBM is suspected since delay is strongly associated with high mortality and morbidity. There is no need to wait for microbiological or molecular diagnostic confirmation. TBM should be suspected if there is a CSF leucocytosis (predominantly lymphocytes), the CSF protein is raised, and the CSF:plasma glucose is $<50\%$.[9] A tissue diagnosis (by histopathology and mycobacterial culture) should be attempted whenever possible, either by biopsy of the lesion itself, or through diagnostic sampling from extraneural sites of disease. The role of CSF diversion in TBM needs to be objectively evaluated since the symptomatology of meningitis frequently overlaps symptoms of raised intracranial procedure. In addition, fundus exam in a patient with TBM can sometimes be misleading due to arachnoiditis surrounding the optic apparatus. Hence a close clinical follow-up is needed to determine the appropriate time for cerebrospinal fluid (CSF) diversion procedure in event of clinical decompensation. The Vellore grading system provides a fair guideline for CSF diversion.[10] CSF diversion procedure should be performed for chronic symptomatic or progressive hydrocephalus. In grade IV TBM, CSF diversion is contemplated only if there is clinical improvement following external ventricular drain insertion. However, Srikantha et al.[11] in a retrospective study comprising of 95 patients conclude that direct VP shunt placement is an effective option in patients with Grade IV TBM with hydrocephalus. Early shunt deployment is known to prevent long-term neurological sequelae.[12,13] An inadvertent delay in the decision making process for CSF diversion can have a deleterious effect on the neuropsychological and cognitive outcome. Endoscopic third ventriculostomy (ETV) is performed in patients who have been treated with antituberculous therapy for at least 4 weeks or in whom the disease is burnt out or onset of hydrocephalus is late in the disease.[14] It is fraught with risks since the floor of the third ventricle may be thick and opaque, thus increasing the risk of injury to basilar artery and its perforators. ETV in TBM and hydrocephalus is technically demanding procedure and requires considerable skill and experience for a successful outcome. The grade at presentation is the best and most consistent predictor of outcome following shunt surgery in patients with TBM.

Fungal infections of the central nervous system (CNS) are rare in the general population and are most frequently encountered in immunocompromised patients such as those with acquired immunodeficiency syndrome or after organ transplantation.[1] Fungal brain abscesses caused by yeast (eg, Candida spp, Cryptococcus spp), dimorphic fungi (eg, Histoplasma spp, Coccidioides spp, Blastomyces spp), and molds (eg, Aspergillus spp, Rhizopus) are associated with immunocompromised states, and in the case of zygomycosis, poorly controlled diabetes.[1,2] Due to the lack of inflammatory response, neuroradiological findings are often nonspecific and are frequently mistaken for tuberculous meningitis, pyogenic abscess or brain tumor. Intracranial fungal infections are being identified more frequently due to the increased incidence of Acquired immunodeficiency syndrome (AIDS) patients, better radiological investigations, more sensitive microbiological techniques and better critical care of moribund patients. Although almost any fungus may cause encephalitis, cryptococcal meningoencephalitis is most frequently seen, followed by aspergillosis and candidiasis. The prognosis of fungal meningitis is dismal. Surgical decompression for large fungal granulomas, especially aspergillus can produce transient improvement due to reduction in the intracranial pressure but eventual outcome is uniformly poor.[1,2] Cryptococcosis is a global invasive mycosis associated with significant morbidity and mortality. Cryptococcal meningoencephalitis is divided into three risk groups viz. human immunodeficiency virus (HIV)-infected individuals, organ transplant recipients, non-HIV-infected and nontransplant hosts.[15] There are specific recommendations for other unique risk populations, such as children, pregnant women, persons in resource-limited environments, and those with Cryptococcus gattii infection. There is a special emphasis on potential complications in management of cryptococcal infection, including increased intracranial pressure, immune reconstitution inflammatory syndrome (IRIS), drug resistance, and cryptococcomas. The management principles include induction therapy for meningoencephalitis using fungicidal regimens, such as a polyene and flucytosine, followed by suppressive regimens using fluconazole, importance of early recognition and treatment of increased intracranial pressure and/or IRIS; and the use of lipid formulations of amphotericin B regimens in patients with renal impairment. Cryptococcosis can be managed successfully in the vast majority of patients if the diagnosis is made early, treatment is instituted according to the guidelines and underlying disease is controlled.[15] CNS cryptococcoma is rare in immunocompetent patients.[16,17] The symptomatology is similar to CNS tumors and can be difficult to diagnose preoperatively. Ring-shaped enhancement of mass lesions with or without cystic changes in the MR imaging may indicate cryptococcoma, but definitive diagnosis relies on pathological study of the lesion specimen. Open surgery and anti-fungal therapy is the treatment of choice.[16,17] The prognosis of cryptococcoma is largely determined by its location. There are many controversies and unresolved issues in neurosurgical practice like minimal invasive versus total resection of the fungal granuloma, fungal intracranial presentation in immunocompetent patients, high mortality of fungal cases managed without antifungal cover, duration of antibiotics, optimal time and mode of hydrocephalus treatment.[16]

Hydatid disease affects a large population around the world and has a potential to cause considerable mortality and morbidity, if not handled properly.[18,19] The epidemiology of echinococcosis is influenced by agricultural, educational, economic, medical and cultural factors. Infection of the central nervous system is rare, and the mainstay of treatment is surgical excision of the intracranial or spinal cyst, when present. Despite all the advances in imaging techniques and therapeutic methods, central nervous system hydatidosis remains difficult to cure and patient outcomes are not satisfactory especially in case of spinal involvement due to the high incidence of recurrence.[19] Cranial hydatid with many daughter cysts is difficult to excise without spillage and recurrence is an inevitable complication. At surgery, a large scalp flap should be raised

overlying the lesion based on imaging, followed by careful handling of the cyst with meticulous technique and follow the Dowling-Orlando technique. In children, although the complications following cerebral hydatid cyst surgery in children are varied, they are not usually fatal, if appropriate surgical therapy is utilized.[20] Surgical removal of the clinically symptomatic cysts and treatment with antihelminthics are only palliative. Prevention is the best strategy and has been successful in New Zealand, Australia, and China. In India, the definitive host is the domestic dog and the intermediate hosts are sheep, goat, and cattle. In a study on the incidence of hydatid infestation in intermediate hosts in Kurnool the positivity of goats, sheep, and cattle was 16.96, 21.75, and 60.94%, respectively.[21] The positivity in dogs in Kurnool region was 33.3%. These facts emphasize the need to control the disease in intermediate hosts and definitive hosts to contain the hydatid disease. Surveillance of dogs and periodic test of the stools is paramount for effective treatment. The access to raw offal at slaughter houses and farms should be prevented to effectively control the incidence of hydatidosis.[21,22]

Neurocysticercosis is the commonest parasitic infestation of the brain. About 50 million people worldwide suffer from this disease.[23] In India; there are one million patients with active epilepsy due to neurocysticercosis. Nearly two-thirds of the patients in India harbor only one degenerating cyst – the solitary cysticercus granuloma which is the commonest cause of focal seizures in Indian patients.[23] Mostly, the therapy of NCC is medical and symptomatic. Cysticidal drugs such as praziquantel and albendazole are also used in the treatment of NCC. Surgery is reserved for selected patients with NCC and plays a minor role in the management of the disease.[23,24] It is usually recommended for intraventricular cysts, hydrocephalus, large cisternal cysts, large parenchymal cysts and when the diagnosis is not certain on imaging studies. Endoscopic surgery is the procedure of choice for intraventricular cysts.[24] Incompletely excised cysts and cysts or granulomas in locations such as the spinal cord can be treated with steroids and albendazole. Although hydrocephalus is treated with a ventriculo-peritoneal shunt but the incidence of frequent obstructions and multiple revisions is high. The outcome for patients with intraventricular and parenchymal cysts is usually good except for patients with hydrocephalus associated with cisternal or racemose cysts.[23,24] The mortality is high in cysticercotic meningitis. The possible strategies to control cysticercosis include health education emphasizing the need for hygienic practices such as hand washing after defecation and before eating, mass chemotherapy for taeniasis and vaccination of pigs. Eradication of the disease is possible but socio-economic factors prevent achievement of this goal in the near future in several under-developed regions of the world.

Pneumocystis carinii (jiroveci) pneumonia has been one of the most important opportunistic infections in AIDS patients.[25] Prophylaxis of Pneumocystis pneumonia is necessary for patients requiring corticosteroids for more than 1 month.[25,26]

Postoperative wound infection (PWI) after intracranial neurosurgery is a significant issue in any neurosurgical unit with a substantial potential for morbidity and mortality, if not addressed proactively. The reported incidence of PWI after intracranial neurosurgery ranges from 1% to 8% in published series.[27] PWI after intracranial neurosurgery was nearly 3 times more likely in European versus North American studies. It highlights the need for future prospective studies to provide evidence-based explanations for these differences. Respiratory tract infections were common in patients following traumatic brain injury who underwent surgery with Acinetobacter spp. being the emerging offending pathogens.[27,28] Device-related postoperative communication of the CSF and the environment is a significant risk factor for and development of meningitis in particular. Malignancy is an independent risk factor for surgical site infection in selected patient populations, hyperglycemia has been shown to increase the risk of surgical site infection whereas stringent glucose control has improved outcomes.[29] Till date, there is no study which has focussed on whether surgical site infection in patients with brain tumors undergoing resection is associated with hyperglycemia. Glucose level is not a significant factor in development of postoperative surgical site infection if duration of surgery and adherence to antibiotic prophylaxis is monitored. However, duration of surgery is significantly associated with postoperative surgical site infection.[29]

In conclusion, central nervous system infections still continue to be a formidable challenge despite introduction of newer and effective antimicrobial chemotherapy. MR imaging should be judiciously used to differentiate brain abscess from tumors and cysts. Prompt institution of intravenous antibiotics and therapeutic drainage of brain abscess should be performed. CSF diversion procedures for postmeningitic hydrocephalus should be performed timely to prevent long-term neurological and cognitive decline. Tuberculosis, Hydatid disease, cryptococcosis, neurocysticercosis, HIV-related CNS infections and postoperative wound infection are still major issues in developing countries. Prevention including health education and good hygienic practices are of paramount importance.

Conflict of interest

None declared.

References

1. Menon S, Bharadwaj R, Chowdhary A, Kaundinya DV, Palande DA. Current epidemiology of intracranial abscesses: a prospective 5 year study. *J Med Microbiol* 2008;**57**:1259–68.
2. Kaczorowska B, Chmielewski H, Pawełczyk M, Przybyła M, Błaszczyk B, Chudzik W. The case of multiple brain abscesses conservatively treated. *Pol Merkur Lekarski* 2007;**22**:150–3 [in Polish].
3. Guzman R, Barth A, Lövblad KO, El-Koussy M, Weis J, Schroth, et al. Use of diffusion-weighted magnetic resonance imaging in differentiating purulent brain processes from cystic brain tumors. *J Neurosurg* 2002;**97**:1101–7.
4. Burtscher IM, Holtas S. In vivo proton MR spectroscopy of untreated and treated brain abscesses. *AJNR Am J Neuroradiol* 1999;**20**:1049–53.
5. Fountas KN, Kapsalaki EZ, Gotsis SD, Kapsalakis JZ, Smisson 3rd HF, Johnston KW, et al. In vivo proton magnetic resonance spectroscopy of brain tumors. *Stereotact Funct Neurosurg* 2000;**74**:83–94.
6. Clark CA, Barrick TR, Murphy MM, Bell BA. White matter fiber tracking in patients with space-occupying lesions of the brain: a new technique for neurosurgical planning? *Neuroimage* 2003;**20**:1601–8.
7. Lee TH, Chang WN, Su TM, Chang HW, Lui CC, Ho JT, et al. Clinical features and predictive factors of intraventricular rupture in patients who have bacterial brain abscesses. *J Neurol Neurosurg Psychiatry* 2007;**78**:303–9.
8. Desai K, Bhatjiwale M, Nadkarni T, Goel A. Flare up of tuberculous abscess following stereotactic aspiration. Case report. *Neurologia Medico-Chirurgica* 2002;**42**:147–9.
9. Thwaites G, Fisher M, Hemingway C, Scott G, Solomon T, Innes J. British infection society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. *J Infect* 2009;**59**:167–87.
10. Palur R, Rajshekhar V, Chandy MJ, Joseph T, Abraham J. Shunt surgery for hydrocephalous in tubercular meningitis: a long-term follow-up study. *J Neurosurg* 1991;**74**:64–9.
11. Srikantha U, Morab JV, Sastry S, Abraham R, Balasubramaniam A, Somanna S, et al. Outcome of ventriculoperitoneal shunt placement in grade IV tubercular meningitis with hydrocephalus: a retrospective analysis in 95 patients. Clinical article. *J Neurosurg Pediatr* 2009;**4**:176–83.
12. Sil K, Chatterjee S. Shunting in tuberculous meningitis: a neurosurgeon's nightmare. *Childs Nerv Syst* 2008;**24**:1029–32.
13. Muzumdar D. Shunting in tuberculous meningitis: a neurosurgeon's nightmare. *Childs Nerv Syst* 2008;**24**:1383–4.
14. Rajshekhar V. Management of hydrocephalus in patients with tuberculous meningitis. *Neurol India* 2009;**57**:368–74.
15. Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of America. *Clin Infect Dis* 2010;**50**:291–322.
16. Li Q, You C, Liu Q, Liu Y. Central nervous system cryptococcoma in immunocompetent patients: a short review illustrated by a new case. *Acta Neurochir (Wien)* 2010;**152**:129–36.

17. Mazumder SA, Cleveland KO. Cryptococcal meningitis after neurosurgery. *Am J Med Sci* 2010;**339**:582–3.
18. Nourbakhsh A, Vannemreddy P, Minagar A, Toledo EG, Palacios E, Nanda A. Hydatid disease of the central nervous system: a review of literature with an emphasis on Latin American countries. *Neurol Res* 2010;**32**:245–51.
19. Limaiem F, Bellil S, Bellil K, Chelly I, Mekni A, Khaldi M, et al. Primary hydatidosis of the central nervous system: a retrospective study of 39 Tunisian cases. *Clin Neurol Neurosurg* 2010;**112**:23–8.
20. Tuzun Y, Solmaz I, Sengul G, Izci Y. The complications of cerebral hydatid cyst surgery in children. *Childs Nerv Syst* 2010;**26**:47–51.
21. Reddy DR. Managing cerebral and cranial hydatid disease. *Neurol India* 2009; **57**:116–8.
22. Dziri C, Haouet K, Fingerhut A, Zaouche A. Management of cystic echinococcosis complications and dissemination: where is the evidence? *World J Surg* 2009;**33**:1266–73.
23. Rajshekhar V. Surgical management of neurocysticercosis. *Int J Surg* 2010;**8**: 100–4.
24. Sinha S, Sharma BS. Neurocysticercosis: a review of current status and management. *J Clin Neurosci* 2009;**16**:867–76.
25. Somand D, Meurer W. Central nervous system infections. *Emerg Med Clin North Am (United States)* 2009;**27**:89–100.
26. Hall WA, Truwit CL. The surgical management of infections involving the cerebrum. *Neurosurgery (United States)* 2008;**62**:519–30.
27. Kourbeti IS, Papadakis JA, Neophytou C, Filippou M, Ioannou A, Karabetsos DA, et al. Infections in patients with traumatic brain injury who undergo neurosurgery. *Br J Neurosurg*; 2010 Jul 22 [Epub ahead of print].
28. Dashti SR, Baharvahdat H, Spetzler RF, Sauvageau E, Chang SW, Stiefel MF, et al. Operative intracranial infection following craniotomy. *Neurosurg Focus (United States)* 2008;**24**(6):E10.
29. Hardy SJ, Nowacki AS, Bertin M, Weil RJ. Absence of an association between glucose levels and surgical site infections in patients undergoing craniotomies for brain tumors. *J Neurosurg* 2010;**113**:161–6.

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30 March 2010
Available online 5 November 2010